



OCTAGON THERAPEUTICS

Antibiotic Innovation.

A collection of medical supplies including a red pill bottle, a syringe, and various pills on a white surface. The red pill bottle is tilted, with its cap removed. The syringe is lying on its side. There are several red and yellow capsules and white pills scattered around. The background is a white surface with some text visible.

Developing targeted medicines for bacterial disease

Antibiotics

Diagnostic accuracy and diversity of modern treatment methods allow
to choose the most effective set of treatment for each patient individual
treatment is not toxic, has no contraindications to repeated
The drug was high compared with standard therapy

CORE TEAM



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Jim Collins, MIT Professor of Biological Engineering

Carbon sources tune antibiotic susceptibility in Pseudomonas aeruginosa via tricarboxylic acid cycle control.

Antibiotic efficacy - context matters.

Antibiotic efficacy is linked to bacterial cellular respiration.



Eric Brown, McMaster University Professor in the Department Biomedical Sciences, M.G. DeGrootte Institute for Infectious Disease Research

The Genome-Wide Interaction Network Of Nutrient Stress Genes In Escherichia Coli.

Unconventional Screening Approaches For Antibiotic Discovery.



Eleftherios Mylonakis, Brown University Professor of Infectious Diseases, Professor of Medicine, Professor of Molecular Microbiology and Immunology

Insect-Derived Cecropins Display Activity against Acinetobacter baumannii in a Whole-Animal High-Throughput Caenorhabditis elegans Model.

A Multi-Host Approach for the Systematic Analysis of Virulence Factors



THERAPEUTIC FOCUS

Current antibiotics are no longer effective against many bacterial pathogens

42% Acinetobacter, 27% Pseudomonas strains now resistant

35% mortality rate for resistant pneumonia

700,000 deaths per year globally due to antibiotic resistance

4.5 million Resistant infections per year (US and EU)

20% Respiratory Infections

20% Urinary Tract Infections

24% Skin and Skin Structure (SSSI) and Surgical Site



CRITICAL MEDICAL NEED

WHO's top 12 priority pathogens for new antibiotics

Priority 1: Critical

- *Acinetobacter baumannii*, carbapenem-resistant
- *Pseudomonas aeruginosa*, carbapenem-resistant
- *Enterobacteriaceae*, carbapenem-resistant, ESBL-producing

Priority 2: High

- *Enterococcus faecium*, vancomycin-resistant
- *Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and resistant
- *Helicobacter pylori*, clarithromycin-resistant

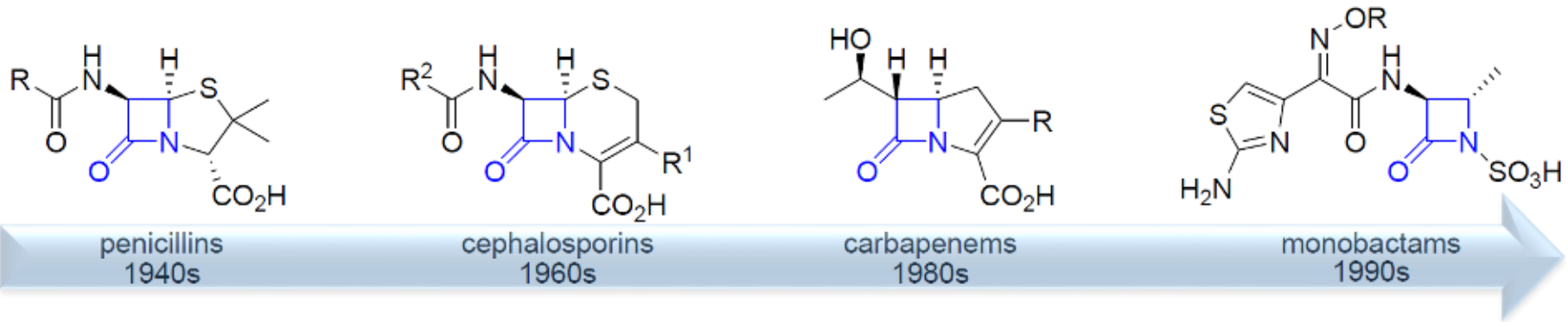
Projected to claim more lives than cancer

Octagon's medicines are effective against the most dangerous bacteria



COMPETITIVE LANDSCAPE

Antibiotic development marked by **iteration and variation** on older compounds



Older classes share **common mechanisms of resistance**

A first-in-class antibiotic has not been approved in decades

Clinical pipeline is extremely limited

Increasing price points, currently \$1500-\$3500 per course

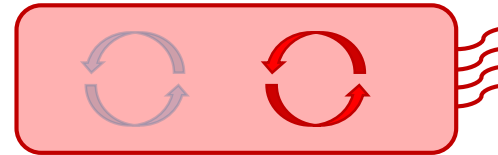
TECHNOLOGY OVERVIEW

Bacteria rely on specific metabolic pathways during an infection

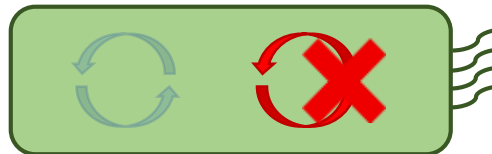
In vitro culture



During infection

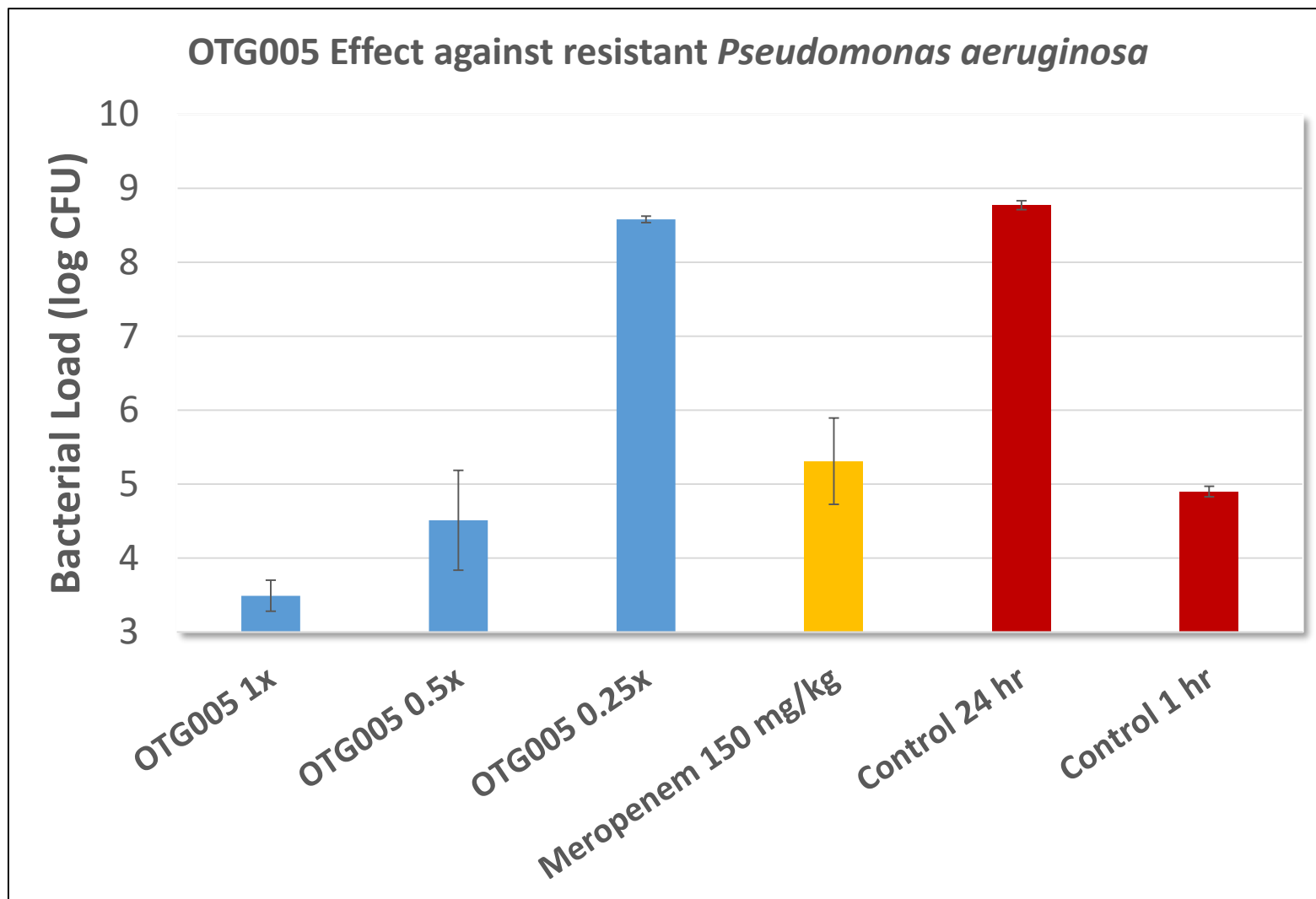


Octagon can induce bacteria to preferentially use these pathways *in vitro*



Has discovered novel small molecule inhibitors invisible to other methods

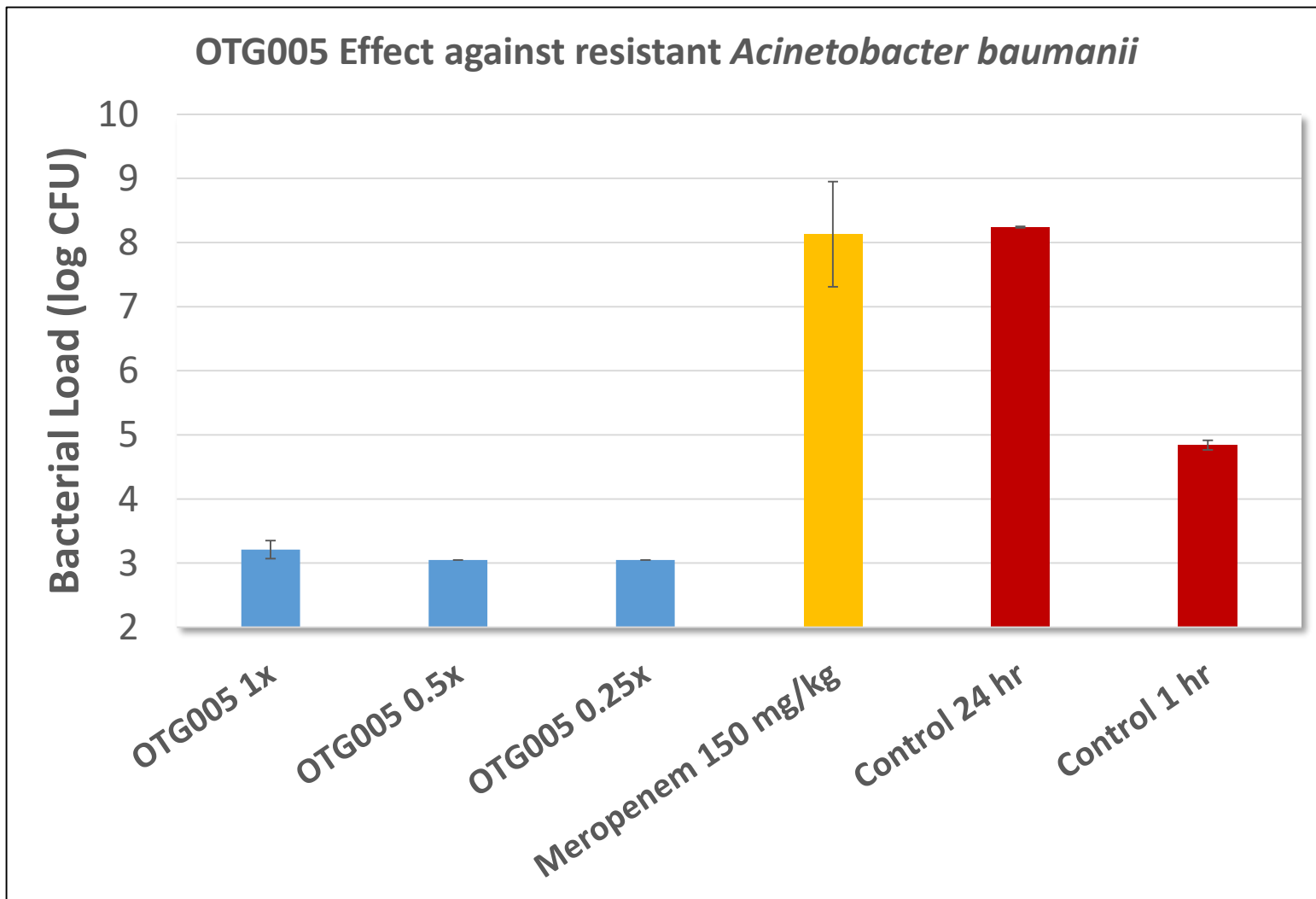
IN VIVO EFFICACY, INFECTED THIGH MODEL



*Resistant clinical strain



IN VIVO EFFICACY, INFECTED THIGH MODEL



*ESBL-expressing clinical isolate

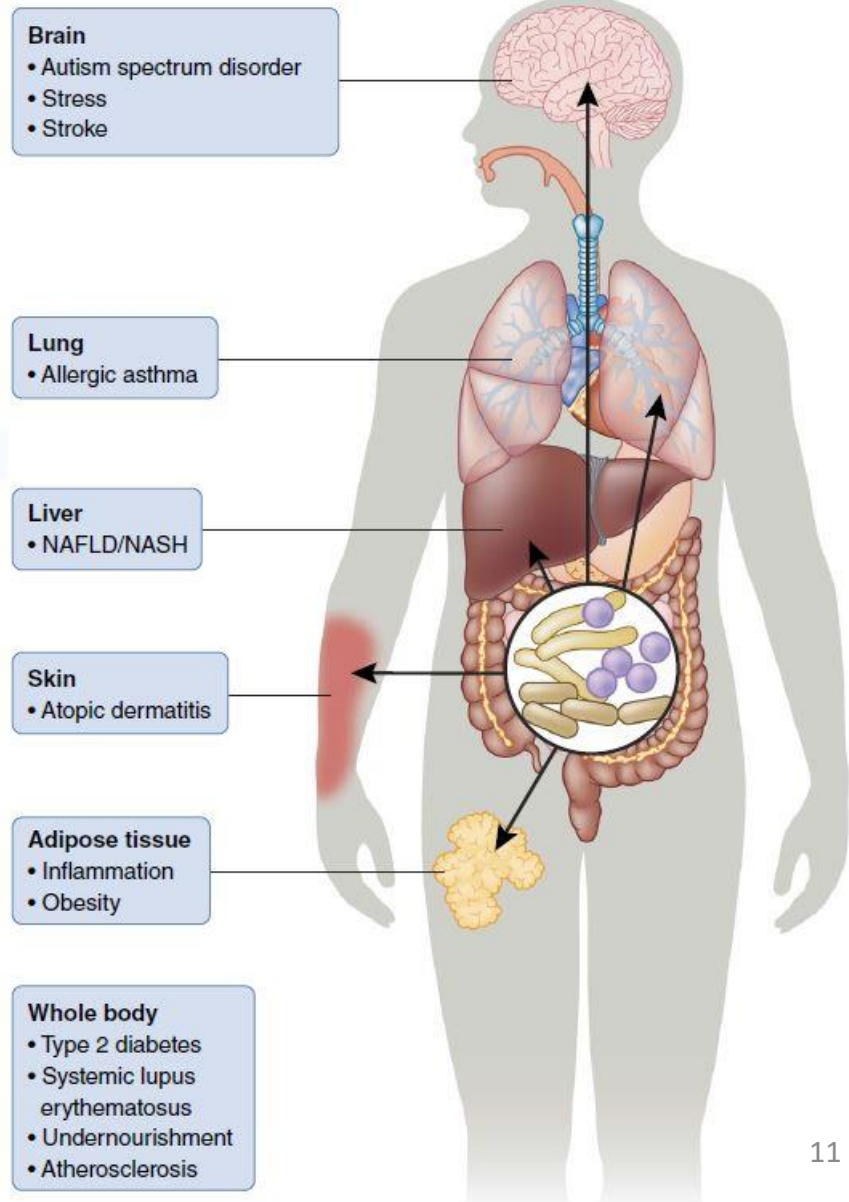


BEYOND INFECTIOUS DISEASE

Microbiome field is dominated by “Bugs as Drugs” paradigm

Octagon specifically targets pathogenic bacteria, sparing commensal strains

Broad platform application into GI, metabolic, CNS indications



CURRENT STATUS

Initiated Financing Process to Support:

Assessment of repurposing candidates identified with screening platform

Protectable drug assets through use patents, formulation

Potential for rapid development through 505(b)(2)

Pharmacophores for chemical optimization

Candidate series based on OTG005

SAR and analog synthesis and evaluation

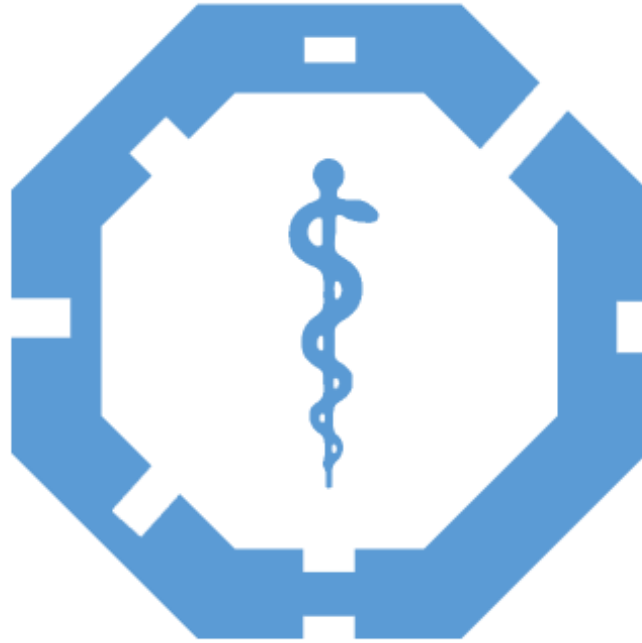
Generating optimized protectable New Chemical Entities

Further screening efforts

Collaboration with industry/academic partners

Differentiated screening approach likely to identify novel hits





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SUPPLEMENTAL: INTELLECTUAL PROPERTY

Initial IP developed at Partners/MGH

Exclusive agreement signed with Partners

Filings cover drug discovery methodology, use of known compounds, efficacious hits generated in initial screen

Represented by Fish and Richardson

IP Generated at Octagon

Composition of matter on novel target inhibitors

Combinations/synergy with legacy antibiotics

Optimized and expanded screening platform

Retained Lathrop-Gage as intellectual property counsel



CLINICAL POSITIONING

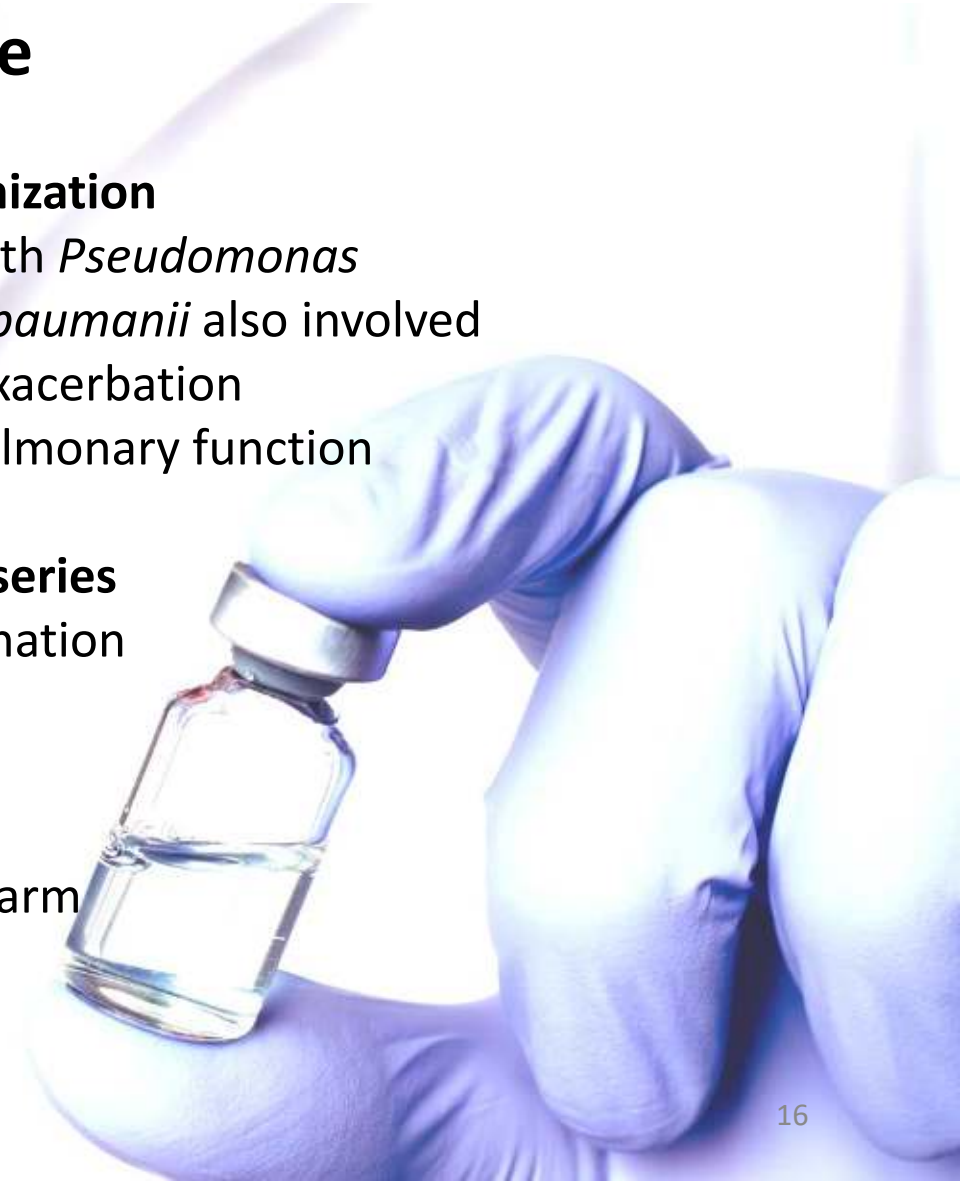
OTG005 Target Product Profile

Cystic Fibrosis-Associated Bacterial Colonization

80% of adult CF Patients colonized with *Pseudomonas Burkholderia cepacia*, *Acinetobacter baumannii* also involved
Recurrent or chronic infection with exacerbation
Eventual terminal deterioration of pulmonary function

Development Candidates based on lead series

Qualifies for GAIN Act, Orphan Designation
Proof-of-efficacy in small Ph1b study
Strong patient advocacy group (CFF)
Expand label into HAP/VAP
Narrow spectrum, less microbiome harm



NONDILUTIVE FINANCING EFFORTS

Ongoing discussions/proposals:



High-level conversations



\$4M R01 Grant Application Pending

CARB-X

Xccelerating global antibacterial innovation

\$2M Proposal in prep



SBIR
America's Seed Fund™

\$0.6M Grant Application Pending



National Institute
of Allergy and
Infectious Diseases

CAP to support development



USAMRIID

United States Army
Medical Research Institute
of Infectious Diseases

Collaboration initiated

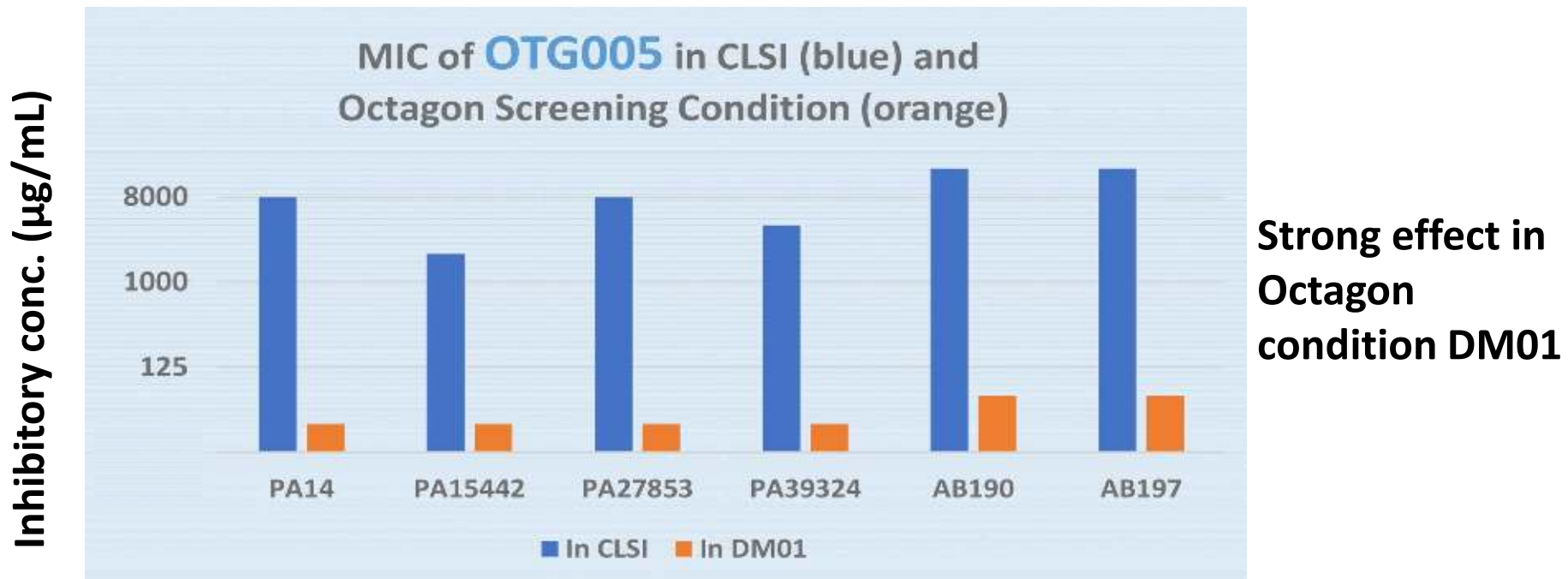


BACTERIAL INHIBITION IN VITRO

Pilot screening campaign, **known bioactives**

19 strong hits identified with the potential to be new antibiotics

OTG005 shown below is a generic medicine, unrelated indication



Many bacterial strains tested

Potential lifesaving medicines are **invisible to standard discovery methods**



SUPPLEMENTAL: INTELLECTUAL PROPERTY

FISH.
FISH & RICHARDSON



Vasily Ignatenko PhD

**LATHROP
GAGE**



Shann Kerner PhD, JD



SUPPLEMENTAL: PROTECTING A REPURPOSED DRUG

Potential for 8-12+ years of US market exclusivity at approval

505(b)(2) NDA

Minimal preclinical toxicology
Streamlined clinical program
3-5 years market access

Orphan Designation

Target population < 200,000 per year
Recent example: iclaprim for Cystic Fibrosis
7 years market access

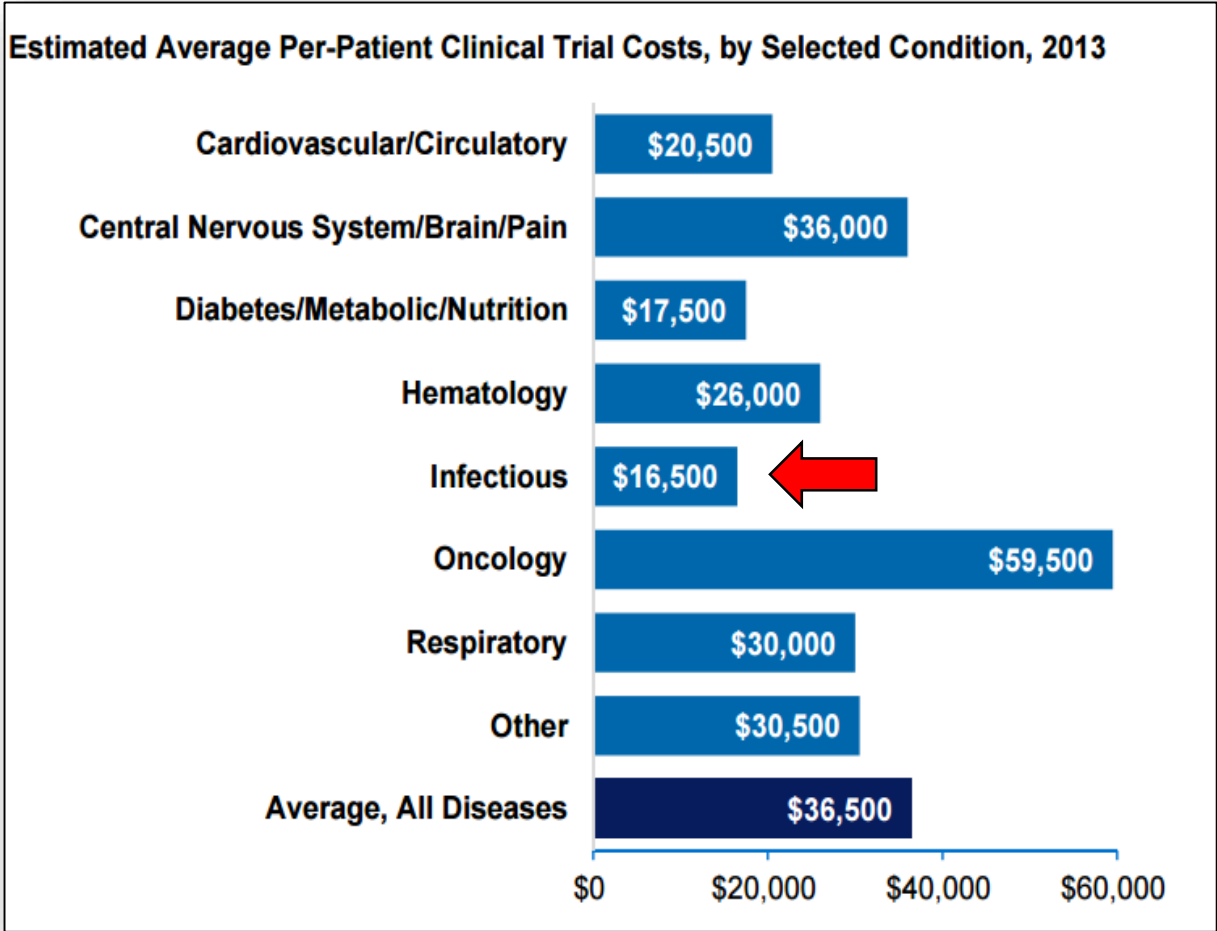
QIDP Under GAIN Act

Acinetobacter, Pseudomonas on pathogen list
5 years market access



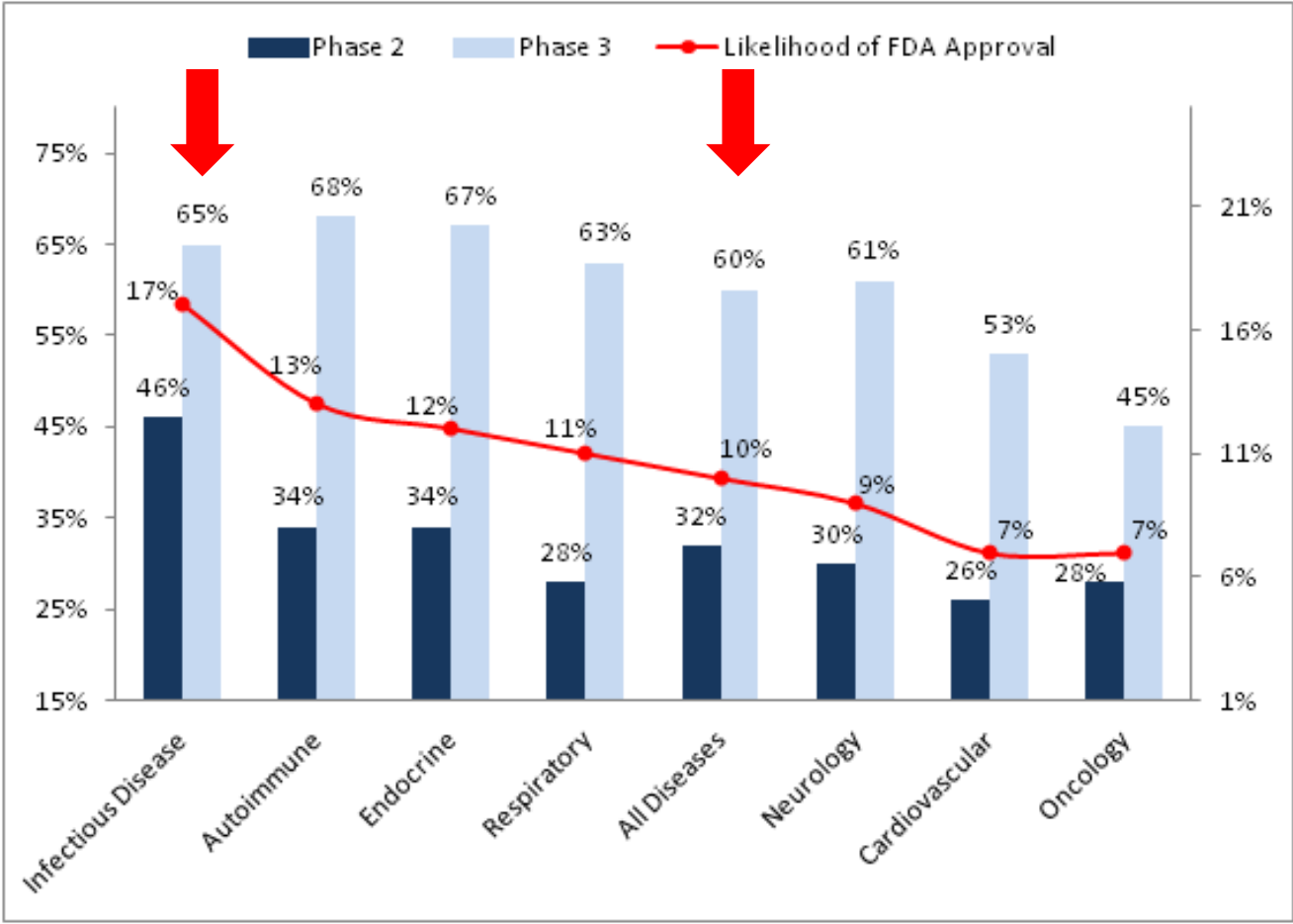
SUPPLEMENTAL

Least costly clinical trials, non-inferiority endpoints



SUPPLEMENTAL

Highest likelihood of approval due to **high predictive power of animal models**



RECENT DEALS

Increasing transaction volume and size

Active players

| |
|------------------------------------|
| Teva Pharmaceutical Industries Ltd |
| Allergan Plc |
| Pfizer Inc |
| Perrigo Company Plc |
| GlaxoSmithKline Plc |
| Roche |
| Merck and co. |

